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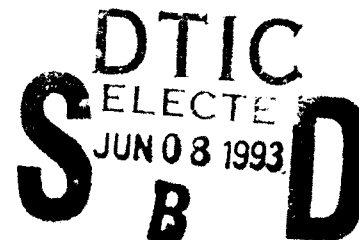
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"The Nonnatural Deoxyribonucleoside D₃ Incorporated in an
Intramolecular DNA Triplex Binds Sequence Specifically by
Intercalation"

by

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Division of Chemistry and Chemical Engineering
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The Nonnatural Deoxyribonucleoside D₃ Incorporated in an Intramolecular DNA Triplex Binds Sequence Specifically by Intercalation

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Abstract: The synthetic deoxyribonucleoside 1-(2-deoxy- β -D-ribofuranosyl)-4-(3-benzamido)phenylimidazole (D₃) has been shown to specifically recognize both T·A and C·G base pairs when incorporated into the Hoogsteen paired strand of pyrimidine·purine·pyrimidine triplexes. To further investigate the binding of D₃, a DNA oligonucleotide containing a single D₃ residue and designed to form intramolecular triplexes was synthesized and studied by one- and two-dimensional NMR spectroscopy. The oligonucleotide d(AGATAGAACCCCTTCTATCTTATATCTD₃TCTT) was found to form a stable intramolecular triplex, with a CCCC and a TATA loop connecting the Watson-Crick and Hoogsteen paired strands, respectively. Unlike other third strand bases, however, D₃ does not hydrogen bond with a Watson-Crick base pair. Instead, it intercalates between its associated base pair (T·A) and the adjacent 3' T·A·T triplet. The binding mode of D₃ is unique in that it not only binds by intercalation but skips a potential base pair to do so. Thus, non-purine bases can be accommodated in the purine strand of DNA triplexes in an entirely new way.

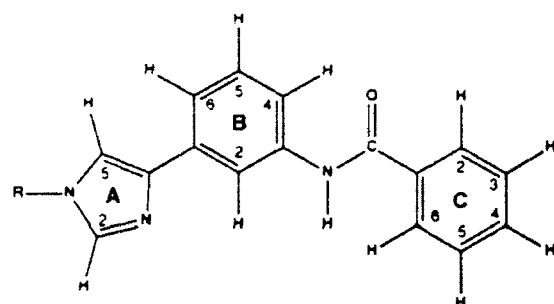
Figure Captions

Figure 1. (A) Chemical structure of the nonnatural deoxyribonucleoside D₃ with ring labeling and numbering scheme used. **R** is deoxyribose. (B) Schematic of the proposed folding of the 31 base intramolecular triplex with base numbering scheme used. Hydrogen bonds are indicated by (-) except for those of protonated C, indicated by (+).

Figure 2. Schematic illustrating the binding mode of D₃ and neighboring nucleotides.

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